A robust method to derive functional neural crest cells from human pluripotent stem cells.

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Public Summary:
Neural crest cells contribute to the development of the heart, the large vessels from the heart, parts of the face, and peripheral nerves that control pain and the function of internal organs. Generating neural crest cells-including specific subpopulations such as cranial, cardiac, and trunk neural crest cells cells-from human pluripotent stem cells will provide a valuable model system to study human development and disease. Here, we describe an improved method for neural crest cell differentiation. By yielding neural crest cells c in a shorter time frame than other published methods, our method provides an ideal model system for further studies of human neural crest cells development and disease.

Scientific Abstract:
Neural crest (NC) cells contribute to the development of many complex tissues of all three germ layers during embryogenesis, and its abnormal development accounts for several congenital birth defects. Generating NC cells-including specific subpopulations such as cranial, cardiac, and trunk NC cells-from human pluripotent stem cells will provide a valuable model system to study human development and disease. Here, we describe a rapid and robust NC differentiation method called "LSB-short" that is based on dual SMAD pathway inhibition. This protocol yields high percentages of NC cell populations from multiple human induced pluripotent stem and human embryonic stem cell lines in 8 days. The resulting cells can be propagated easily, retain NC marker expression over multiple passages, and can spontaneously differentiate into several NC-derived cell lineages, including smooth muscle cells, peripheral neurons, and Schwann cells. NC cells generated by this method represent cranial, cardiac and trunk NC subpopulations based on global gene expression analyses, are similar to in vivo analogues, and express a common set of NC alternative isoforms. Functionally, they are also able to migrate appropriately in response to chemoattractants such as SDF-1, FGF8b, and Wnt3a. By yielding NC cells that likely represent all NC subpopulations in a shorter time frame than other published methods, our LSB-short method provides an ideal model system for further studies of human NC development and disease.